U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

AD-A036 162

THE RELATIONSHIP BETWEEN THE CONCENTRATIONS OF SERUM LIPOPROTEINS AND SERUM LIPIDS

SCHOOL OF AVIATION MEDICINE
RANDOLPH AIR FORCE BASE, TEXAS

MARCH 1959

ADA036162

(1)

Volanti Subvenimus

f9M

THE RELATIONSHIP BETWEEN THE CONCENTRATIONS OF SERUM LIPOPROTEINS AND SERUM LIPIDS

BERNARD S. SCHLESSINGER, First Lieutenant, USAF (MSC)*
MARGARET F. ALLEN, M. S.†
FREDRICK H. WILSON, JR., B. S.*
LAWRENCE J. MILCH, Colonel, USAF*

*Department of Pharmacology and Biochemistry
†Department of Biometrics

59-45

Air University
SCHOOL OF AVIATION MEDICINE, USAF
RANDOLPH AFB, TEXAS
March 1959

THE RELATIONSHIP BETWEEN THE CONCENTRATIONS OF SERUM LIPOPROTEINS AND SERUM LIPIDS

In this laboratory current research procedures require that simultaneous measurements of blood lipoproteins and blood lipids be accomplished in an effort to estimate the risk of coronary disease. It has been suggested that little additional information is gained by the multiple determinations. These studies report (1) the extent of correlation between ultracentrifugally determined serum lipoproteins, (2) the errors of measurement involved in all determinations, and (3) age-specific values for all serum parameters in the same population. It was found that although a high correlation exists between a linear combination of ultracentrifugally determined lipoproteins and the serum concentrations of cholesterol and phospholipid, the prediction of lipoprotein levels from the purely chemical measurements is not entirely satisfactory. Therefore, for the time being at least, all measurements will have to be accomplished.

In 1950, Gofman (1) reported that the serum lipoprotein concentrations determined by ultracentrifugation were significantly correlated with the incidence of coronary disease in the American male. Subsequently, the utility of such measurements as diagnostic and predictive measures of coronary disease has been the subject of extensive evaluation (2-7). Age-specific values for the concentrations of the standard lipoprotein classes have been recorded (8). This report will compare the measurement errors involved in the estimation of serum concentrations of lipids and lipoproteins; will estimate the extent of correlation between ultracentrifugally determined serum lipoproteins and the corresponding concentrations of cholesterol and lipid phosphorus; and will indicate age-specific values for such serum parameters in the same population.

EXPERIMENTAL

In order to study measurement errors and the correlations between parameters, sera from 20 normal (N) subjects and 20 persons with a proven history of myocardial infarction (MI) were used. All the tests on these samples were performed in duplicate.

The age-specific data were accumulated during the period 1953-1957 from various service agencies.[1] The total number of subjects involved was 1,423. From these data various statistics were computed and are reported below.

The sera were analyzed for the ultracentrifugal concentrations of the S_f^0 0-12, S_f^0 12-20, and S_f^0 20-400 lipoproteins by methods described elsewhere (9-11). In addition, the atherogenic index (A.I.) was calculated.[2] Serum cholesterol concentrations were measured by the Bloor method (12), and lipid phosphorus levels were determined by the Fiske-Subbarow technic (13).

RESULTS AND DISCUSSION

The measurement errors determined from duplicate analyses of lipid and lipoprotein parameters for the 20 N and 20 MI subjects are recorded in table I. The differences between the means of the MI and N groups for each variable are statistically significant and confirm data previously reported (15). The measurement errors[3] are roughly equivalent for the

Received for publication on 14 November 1958.

[1]The breakdown of the group shows 459 West Point cadets, 199 Army basic trainees, 348 Pentagon officers, 228 Air Defense Command personnel, 105 officers referred to the School of Aviation Medicine Consultation Service, and 84 School of Aviation Medicine personnel.

[2]A.I. =

$$\frac{\text{Concentration } (S_f^0\ 0\text{-}12) + 1.75 \text{ concentration } (S_f^0\ 12\text{-}20 + S_f^0\ 20\text{-}400)}{10}$$

(Ref. 14).

[3]The measurement error, in percent, is defined as the within-subject standard deviation divided by the mean of the first determination and multiplied by 100.

TABLE I

Means, standard deviations, and measurement errors for serum parameters in 20 MI's and 20 N's

Variable	Mean		Standard deviation		Measurement error (%)	
	MI	N	MI	N	MI	N
S_f^o 0-12	462	375	122	84	8.5	11.3
S_f^o 12-20	63	45	35	22	19.1	9.6
S_f^o 20-400	155	125	110	101	18.0	14.5
S_f^o 0-400	680	545	207	165	9.8	10.2
A.I.	85	67	29	25	10.7	9.9
Cholesterol	326.4	270.3	73.7	44.6	1.9	2.0
Phospholipid	11.65	10.30	2.45	1.25	3.8	3.8

TABLE II

Correlation coefficients (r) between A.I. and serum parameters

Variable (Y)	$r_{A.I. \cdot Y}$
0-12	.669
12-20	.655
20-400	.894
A.I.'	.916
Cholesterol	.779
Phospholipid	.801

MI and N groups. For ultracentrifugally determined lipoproteins, this error ranges from 8.5 to 19.1 percent; for lipid phosphorus, approximately 4 percent; and for cholesterol, 2 percent.

The correlations between A.I. and the other parameters are given in table II. The duplicate determinations of A.I. gave a correlation of 0.916, somewhat less than the largest obtainable value of 1.00. All other correlations reported are less than 0.916.

Since the correlations between A.I. and other serum parameters are high, and also since the measurement errors of some of these variables are as small as or smaller than those for

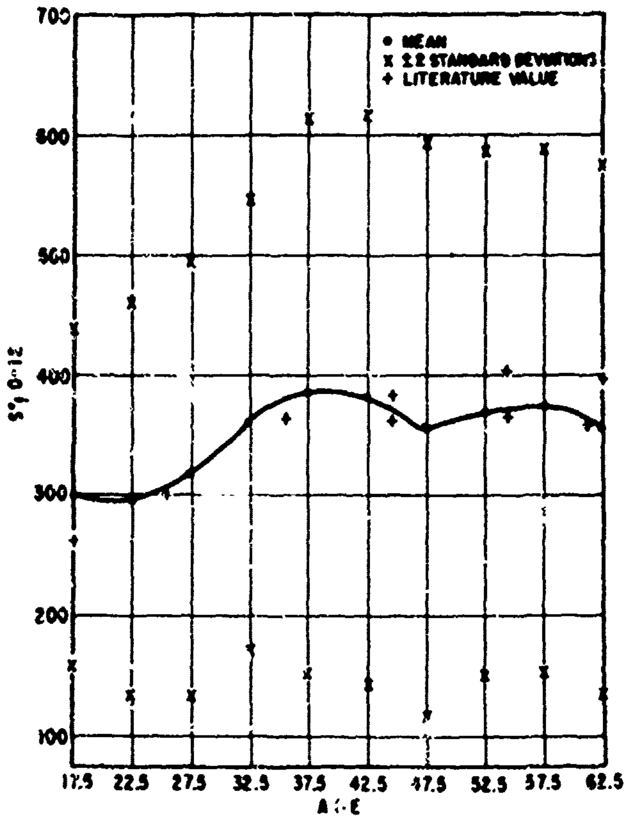

FIGURE 1

Age trend of S_f^o 0-12 lipoprotein concentrations.

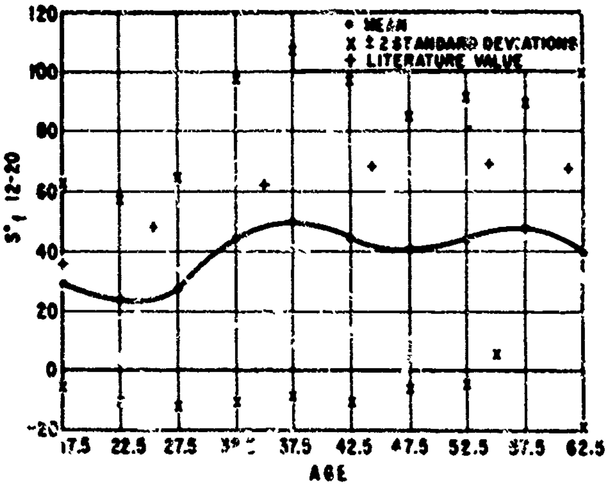

FIGURE 2

Age trend of S_f^o 12-20 lipoprotein concentrations.

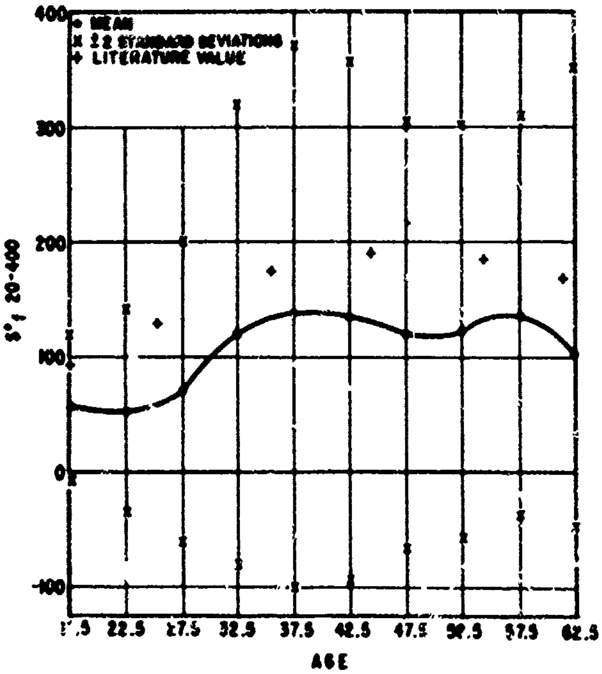

FIGURE 3

Age trend of S_f^o 20-400 lipoprotein concentrations.

A.I., it seemed appropriate to ascertain whether A.I. might be satisfactorily predicted from a linear combination of some or all of these other variables. The data on the 1,423 subjects were used to formulate equations which predicted A.I. from combinations of the three

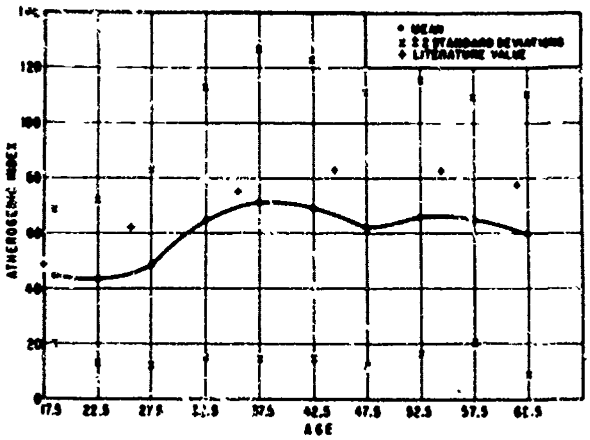

FIGURE 4

Age trend of atherogenic index values.

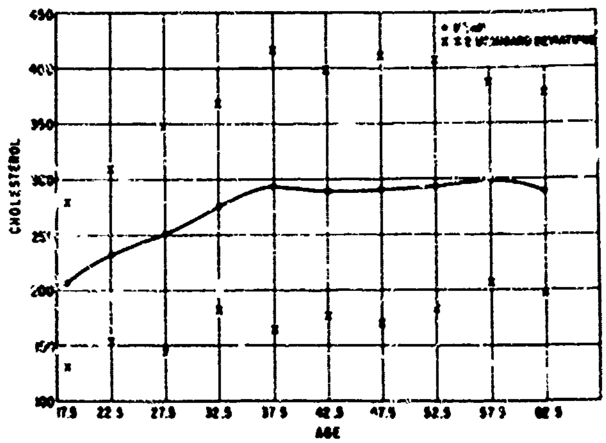

FIGURE 5

Age trend of cholesterol concentrations.

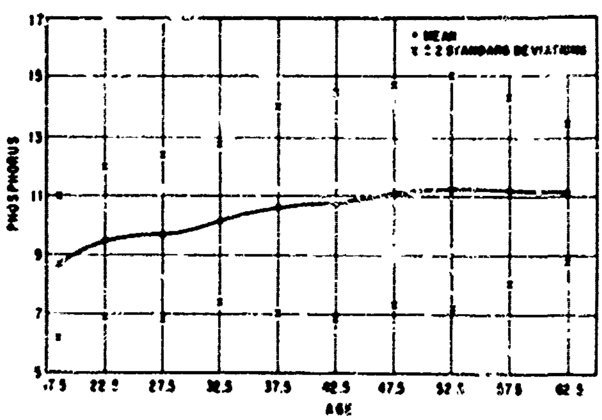

FIGURE 6

Age trend of lipid phosphorus values.

TABLE III

Age distribution of 1,423 subjects

Age group	Number
17-19	70
20-24	509
25-29	145
30-34	35
35-39	117
40-44	186
45-49	195
50-54	111
55-59	37
60-64	18
	1,423

parameters *age, cholesterol,* and *lipid phosphorus.* The best such equation made use of all three parameters and took the form:

$$\text{A.I. (predicted)} = -26.48 + .1661 \text{ age} + .1947 \text{ cholesterol} + 2.4906 \text{ lipid phosphorus.}$$

This equation was used to estimate A.I. from the first run determinations of cholesterol and lipid phosphorus for the N and MI groups totaling 39 samples. These predicted A.I. values were correlated with both A.I. and A.I.'; the correlation coefficients were .800 and .816, respectively. It is evident that there is better agreement between the duplicate measurements of A.I. than between A.I. and the A.I. predicted from the given equation.

The age-specific values for S_f^o 0-12, S_f^o 12-20, S_f^o 20-400, A.I., cholesterol, and lipid phophorus are presented in figures 1 through 6. The x's indicate two standard deviations from the mean. The +'s are points obtained from the literature (8). Table III gives the age breakdown of the 1,423 persons included in the study.

If the assumption is made that these cross-sectional data are indicative of age changes in the individual, such data then predict that all the lipoprotein concentrations and the cholesterol level will increase at comparable rates during the third and fourth decades of life, after which levels will be maintained. Serum lipid phosphorus concentrations increase at a less rapid rate in an almost linear fashion, but the increase is maintained until the individual is past 50 years of age. The slightly decreased levels in the oldest age group may represent the process of natural selection.

In general, the Gofman lipoprotein data for a civilian population are significantly higher than the data reported here for the military group. These differences may be attributed to the selection which attends induction into the service.

REFERENCES

1. Gofman, J. W., F. Lindgren, H. Elliot, W. Mantz, J. Hewitt, B. Strisower, and V. Herring. The role of lipids and lipoproteins in atherosclerosis. Science 111:166-171 (1950).

2. Experimental studies on the etiology of atherosclerosis. (Editorial) J. A. M. A. 143:1344 (1950).

3. Gertler, M. M., and S. M. Garn. Lipid interrelationship in health and in coronary artery disease. Science 112:14-16 (1950).

4. Oliver, M. F., and G. S. Boyd. Serum lipoprotein patterns in coronary sclerosis and associated conditions. Brit. Heart J. 17:299-302 (1955).

5. Lewis, L. A., and I. H. Page. Ultracentrifuge and electrophoretic studies on serum lipoproteins in relationship to vascular disease. Circulation 2:466 (1950).

6. Gertler, M. M., S. M. Garn, and P. D. White. Young candidates for coronary heart disease. J. A. M. A. 147:621-625 (1951).

7. Report of a cooperative study of lipoproteins and atherosclerosis: Evaluation of serum lipoprotein and cholesterol measurements as predictors of clinical complication of atherosclerosis. Circulation 14:691-743 (1956).

8. Gofman, J. W., O. deLalla, N. K. Glazier, F. T. Lindgren, A. V. Nichols, B. Strisower, and A. R. Tamplin. The serum lipoprotein transport system in health, metabolic disorders, atherosclerosis, and coronary heart disease. Plasma 2, No. 4:413-484 (1954).

9. Redmond, R. F., L. J. Milch, W. W. Calhoun, H. I. Chinn, and the Cardiovascular Research Group. The evaluation of clinical tests for atherosclerosis. I. Instrumentation. School of Aviation Medicine, USAF, Project No. 21-32-027, Report No. 1, Aug. 1952.

10. Milch, L. J., W. W. Calhoun, and R. F. Redmond. The evaluation of clinical tests for atherosclerosis. Improved techniques in ultracentrifugal analysis. School of Aviation Medicine, USAF, Project No. 21-1601-0007, Report No. 2, Aug. 1953.

11. deLalla, O. F., and J. W. Gofman. Ultracentrifugal analysis of serum lipoproteins. *In* Glick, D. (ed.) Methods of biochemical analyses. New York: Interscience Publishers, Inc., 1954.

12. Robinson, L. G., and E. R. Pugh. The determination of serum cholesterol. U. S. Armed Forces Med. J. 9:501-506 (1958).

13. Redmond, R. F., L. J. Milch, W. W. Calhoun, H. I. Chinn, and the Cardiovascular Research Group. Biochemical and biophysical methods in cardiovascular research. Texas Rep. Biol. and Med. 11:83-109 (1953).

14. Gofman, J., B. Strisower, O. deLalla, A. Tamplin, H. Jones, and F. Lindgren. Index of coronary atherogenesis. Mod. Med. 11:119-140 (1953).

15. Schlessinger, B. S., F. H. Wilson, Jr., L. J. Milch, and the Cardiovascular Research Group. Serum parameters as discriminators between normal and coronary groups. Circulation 19:265 (1959).